Remarks

The claims are 1, 2, 4, 8, 9, 11, and 12. The claims have been amended to recite A being a thiazolyl ring, as described in the specification at, for example, page 11, lines 6-13; the amino acid receptor being metabotropic glutamate as described in the specification at, for example, page 21, lines 13-21; and the disease state being pain, as described in the specification at, for example, page 7, lines 9-18. Accordingly, the changes are not new matter.

I. Rejections Under 35 USC 112

The claims have been rejected as allegedly not described in the specification to enable one in the art to make/use the invention. To expedite prosecution, Applicants have amended the claims to recite A being thiazolyl, the amino acid receptor being metabotropic glutamate, and the disease state being pain.

Applicants respectfully reserve the right to submit claims to the deleted subject matter in a continuing or divisional application.

Accordingly, Applicants respectfully submit that the rejections have been overcome and request their withdrawal.

II Rejections Under 35 USC 103

The claims have been rejected as allegedly obvious over U.S. Patent No. 5,574,036 (the '036 reference) or U.S. Patent No. 6,150,413 (the '413 reference). Applicants respectfully submit that neither the '036 reference or the '413 reference anticipates or makes obvious the claims, as presently amended.

Neither the '036 reference or the '413 reference includes the thiazolyl A group presently required by independent claims 1, 4, 9, and 11. The '036 or '413 reference does not describe, disclose, suggest, teach, or motivate the thiazolyl compounds of the present application as claimed in independent claims 1, 4, 9, and 11, or their use to mediate excitatory neurotransmitter metabotropic glutamate receptors of the mammalian central nervous system. Accordingly, the '036 or '413 references do not make obvious independent claims 1, 4, 9, and 11. Claims 2, 8, and 12, depending from the independent claims, are also not made obvious for that reason as well as for the additional limitations they contain.

Applicants respectfully submit that the rejections have been overcome and request their withdrawal.

Conclusion

Applicants respectfully submit that the application is in condition for allowance and request a Notice to that effect. Attorney for Applicants can be reached at the telephone number and address below. Correspondence should be sent to the address below. Any additional fees or deficiency in fees required should be taken from Merck Deposit Account No. **13-2755**.

Respectfully submitted,

By

Shu M. Lee
Reg. No. 41,147
Attorney for Applicants

MERCK & CO., Inc.
P.O. Box 2000
Rahway, New Jersey 07065-0907
(732) 594-2675

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231, on the date appearing below.

MERCK & CO., INC.

By Shu M. Lee Date May 13, 2002

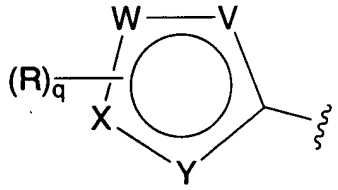
Date: May 13, 2002

CLAIMS MARKED-UP TO SHOW CHANGES

Claim 1. (Amended Thrice) A method of modulating the activity of [excitatory amino acid] metabotropic glutamate receptors, said method comprising:

contacting said receptors with at least one compound having the structure **A-L-B** or enantiomers, diastereomeric isomers or mixtures of any two or more thereof, or pharmaceutically acceptable salts thereof, in an amount sufficient to modulate the activity of said excitatory amino acid receptor, wherein:

A is [a 5-membered ring having the structure:



wherein at least one of **V** and **Y** is CH or CR;

at least one of **V**, **W**, **X**, and **Y** is $(CR)_p$, wherein p is 1;

at least one of **V**, **W**, **X**, and **Y** is S;

the remainder of **V**, **W**, **X**, and **Y** are each N; and

each **R** is independently] thiazolyl optionally substituted with 1 or 2 independent halogen, substituted or unsubstituted hydrocarbyl, substituted or unsubstituted aryl, heterocycle, mercapto, nitro, carboxyl, carbamate, carboxamide, hydroxy, ester, cyano, amine, amide, amidine, amido, sulfonyl or sulfonamide[, wherein q is 0, 1, or 2];

L is alkynylene; and

B is substituted or unsubstituted aryl.

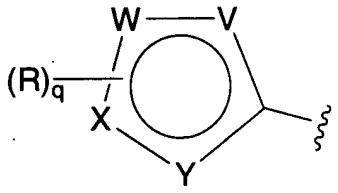
Claim 2. (Amended Twice) The method according to claim 1, wherein said excitatory amino acid receptor is a Group 1 metabotropic glutamate receptor.

Claim 4. (Amended Thrice) A method for treating metabotropic glutamate disease conditions, said method comprising:

administering to a patient having a disease condition a therapeutically effective amount of at least one compound having the structure **A-L-B** or enantiomers, diastereomeric

isomers or mixtures of any two or more thereof, or pharmaceutically acceptable salts thereof, wherein:

A is [a 5-membered ring having the structure:



wherein at least one of **V** and **Y** is CH or CR;
at least one of **V**, **W**, **X**, and **Y** is $(CR)_p$, wherein p is 1;
at least one of **V**, **W**, **X**, and **Y** is S;
the remainder of **V**, **W**, **X**, and **Y** are each N; and
each **R** is independently] thiazolyl optionally substituted with 1 or 2 independent halogen, substituted or unsubstituted hydrocarbyl, substituted or unsubstituted aryl, heterocycle, mercapto, nitro, carboxyl, carbamate, carboxamide, hydroxy, ester, cyano, amine, amide, amidine, amido, sulfonyl or sulfonamide[, wherein q is 0, 1, or 2];

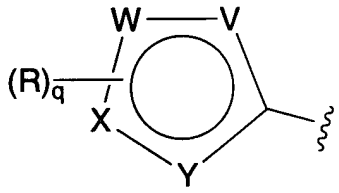
L is alkynylene; and
B is substituted or unsubstituted aryl.

Claim 8. (Amended Twice) The method according to claim 4 [5], wherein said [pain disorder] disease condition is neuropathic pain, chronic pain, acute pain, painful diabetic neuropathy, post-herpetic neuralgia, cancer-associated pain, pain associated with chemotherapy, pain associated with spinal cord injury, pain associated with multiple sclerosis, causalgia and reflex sympathetic dystrophy, phantom pain, post-stroke (central) pain, pain associated with HIV or AIDS, trigeminal neuralgia, lower back pain, myofacial disorders, migraine, osteoarthritic pain, postoperative pain, dental pain, post-bum pain, pain associated with systemic lupus, entrapment neuropathies, painful polyneuropathies, ocular pain, pain associated with inflammation or pain due to tissue injury.

Claim 9. (Amended Thrice) A method for preventing pain [disease conditions] in a subject at risk thereof, said method comprising:

administering to said subject a therapeutically effective amount of at least one compound having structure **A-L-B** or enantiomers, diastereomeric isomers or mixtures of any two or more thereof, or pharmaceutically acceptable salts thereof, wherein:

A is [a 5-membered ring having the structure:

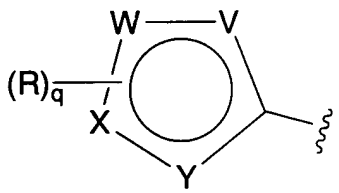


wherein at least one of **V** and **Y** is CH or CR;
at least one of **V**, **W**, **X**, and **Y** is $(CR)_p$, wherein p is 1;
at least one of **V**, **W**, **X**, and **Y** is S;
the remainder of **V**, **W**, **X**, and **Y** are each N; and
each **R** is independently] thiazolyl optionally substituted with 1 or 2 independent halogen, substituted or unsubstituted hydrocarbyl, substituted or unsubstituted aryl, heterocycle, mercapto, nitro, carboxyl, carbamate, carboxamide, hydroxy, ester, cyano, amine, amide, amidine, amido, sulfonyl or sulfonamide[, wherein q is 0, 1, or 2];

L is alkynylene; and
B is substituted or unsubstituted aryl.

Claim 11. (Amended Thrice) A pharmaceutically acceptable salt form of a compound, said compound having the formula **A-L-B** or enantiomers, diastereomeric isomers or mixtures of any two or more thereof, wherein:

A is [a 5-membered ring having the structure:



wherein at least one of **V** and **Y** is CH or CR;
at least one of **V**, **W**, **X**, and **Y** is $(CR)_p$, wherein p is 1;
at least one of **V**, **W**, **X**, and **Y** is S;

the remainder of **V**, **W**, **X**, and **Y** are each N; and

each **R** is independently] thiazolyl optionally substituted with 1 or 2 independent halogen, substituted or unsubstituted hydrocarbyl, substituted or unsubstituted aryl, heterocycle, mercapto, nitro, carboxyl, carbamate, carboxamide, hydroxy, ester, cyano, amine, amide, amidine, amido, sulfonyl or sulfonamide[, wherein q is 0, 1, or 2];

L is alkynylene; and

B is substituted or unsubstituted aryl; and

the salt is acetate, adipate, alginate, aspartate, benzoate, benzenesulfonate, butyrate, citrate, camphorate, camphorsulfonate, cyclopentanepropionate, digluconate, dodecylsulfate, ethanesulfonate, fumarate, glucoheptanoate, glycerophosphate, heptanoate, hexanoate, 2-hydroxyethanesulfonate, lactate, malate, maleate, methanesulfonate, 2-naphthalenesulfonate, nicotinate, oxalate, tartrate, toluenesulfonate, undecanoate, sulfate, bisulfate, hemisulfate, hydrochloride, hydrobromide, hydroiodide, an ammonium salt, an alkali metal salt, an alkaline earth metal salt, a dicyclohexylamine salt, N-methyl-D-glucamine, phenylethylamine, or an amino acid salt.